

CLAIMS

We claim:

1. A variant APRIL protein which modulates at least one BAFF or APRIL biological activity comprising at least one amino acid substitution at a position selected from the group consisting of: 131, 132, 133, 138, 139, 140, 143, 144, 146, 148, 151, 160, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 186, 187, 188, 189, 190, 192, 194, 195, 196, 197, 198, 200, 202, 205, 206, 207, 208, 228, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 271, 273, 275, 276, 278, 282, 284, and 285.
2. A variant APRIL protein according to claim 1, wherein:
 - a) at least one position is modified in an APRIL domain selected from the the group consisting of the Large Domain, Small Domain, and the DE Loop; and
 - b) said modification occurs at a position selected from the group consisting of 138, 139, 140, 170, 171, 172, 173, 174, 175, 176, 177, 178, 180, 181, 186, 187, 188, 189, 195, 196, 197, 198, 205, 206, 207, 208, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, and 240.
3. A variant APRIL protein according to claim 1, wherein said biological activity is selected from the group consisting of modulation of antagonist activity, modulation of BAFF receptor interactions, modulation of APRIL receptor interactions, modulation of BAFF receptor specificity, and APRIL receptor specificity.
4. A variant APRIL protein according to claim 3, wherein modulation receptor binding is selected from at least one of the group consisting of: increase in BAFF-R binding, decrease in BAFF-R binding, increase in TACI binding, decrease in TACI binding, increase in BCMA binding, decrease in BCMA binding.
5. A variant APRIL protein according to claim 4, wherein said biological activity is decreased BAFF-R binding, and said substitution is selected from at least one position in the group consisting of: 131, 133, 173, 175, 176, 177, 179, 181, 192, 195, 197, 230, 231, 233, and 241.
6. A variant APRIL protein according to claim 4, wherein said biological activity is increased BAFF-R binding, and said substitution is selected from at least one position in the group consisting of: 131, 132, 133, 173, 181, 197, 202, 206, 208, 232, and 235.
7. A variant APRIL protein according to claim 4, wherein said biological activity is increased TACI binding, and said substitution is selected from at least one position in the group consisting of: 131, 132, 133, 173, 181, 197, 202, 206, 208 and 232.

8. A variant APRIL protein according to claim 4, wherein said biological activity is decreased TACI binding, and said substitution is selected from at least one position in the group consisting of: 131, 133, 173, 174, 175, 176, 177, 179, 181, 192, 195, 197, 230, 231, and 241,
9. A variant APRIL protein according to claim 4, wherein said biological activity is decreased BCMA binding, and said substitution is selected from at least one of the group consisting of: 131, 133, 173, 174, 175, 176, 177, 179, 181, 192, 195, 197, 206, 208, 230, 231, 232, 237, and 241.
10. A variant APRIL protein according to claim 4, wherein said biological activity is increased BCMA binding, and said substitution is selected from at least one of the group consisting of: 131, 132, 133, 173, 176, 181, 192, 197, 202, 206, 208, and 239.
11. A variant APRIL protein according to claim 4, wherein said antagonist activity is dominant negative antagonism or receptor antagonism.
12. A variant APRIL protein according to claim 11, wherein at least one position is selected from the group consisting of: 143, 144, 146, 148, 172, 174, 192, 194, 196, 198, 200, 206, 207, 228, 230-237, 240-250, 271, 273, 275, 276, 278, 282, 284, and 285.
13. A variant APRIL protein according to claim 1, wherein said variant APRIL protein further comprises a chemical modification.
14. A variant APRIL protein according to claim 13, wherein said chemical modification is made at at least one of the following positions: 131, 132, 146, 151, 160, 175, 190, 233 and 235.
15. A variant APRIL protein according to claim 14, wherein said chemical modification is PEGylation.
16. A pharmaceutical composition comprising a variant APRIL protein according to claim 1 and a pharmaceutical carrier.
17. A recombinant nucleic acid encoding a variant APRIL protein of claim 1.
18. An expression vector comprising the recombinant nucleic acid of claim 17.
19. A host cell comprising the recombinant nucleic acid of claim 17.
20. A host cell comprising the expression vector of claim 18.

21. A method of producing a variant APRIL protein comprising culturing the host cell of claim 19 under conditions suitable for expression of said nucleic acid.
22. The method according to claim 21 further comprising recovering said variant APRIL protein.
23. A method of forming a mixed oligomer comprising a variant APRIL protein of claim 1 with a BAFF protein.
24. A method according to claim 23 wherein said BAFF protein is a variant BAFF protein.
25. A method for treating a BAFF or APRIL-related disorder comprising administering a variant APRIL protein according to claim 1 to a patient in need of said treatment.